

### **REMARKS**

Reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks herein, is respectfully requested. Claims 1 and 8 are amended, and claims 85-91 are added; as a result, claims 1-91 are now pending in this application. The amendments are intended to advance the application and are not intended to concede to the correctness of the Examiner's position or to prejudice the prosecution of the claims prior to amendment, which claims are present in a continuation of the present application.

The Examiner rejected claims 1-5, 8-10 and 14 under 35 U.S.C. § 102(b) as being anticipated by Grant et al. (*J. Biomol. Screening*, 7:531 (2002)). The Examiner also rejected claims 1-14 under 35 U.S.C. § 103(a) as being unpatentable over Grant et al. in view of Bronstein et al. (U.S. Patent No. 6,586,196). These rejections, as they may be maintained with respect to the pending claims, are respectfully traversed.

Grant et al. disclose a dual substrate assay for leucine aminopeptidase and dipeptidyl aminopeptidase that employs Leu-AMC and Gly-Pro-AMC as respective substrates therefor, and a tandem substrate assay for leucine aminopeptidase and dipeptidyl aminopeptidase that employs symmetric bis-(Leu-Ala-Pro)<sub>2</sub>-Rho110 and asymmetric Ala-Pro-Rho110-Leu as substrates. Grant et al. do not teach or suggest a combined bioluminogenic and fluorogenic assay.

Bronstein et al. disclose a method to measure the activity of multiple enzymes, where at least one enzyme is endogenous and at least one enzyme is capable of reacting with a dioxetane (yielding chemiluminescence) (column 3, line 65-column 4, line 5), or where the enzymes are selected from the group consisting of reporter enzymes and endogenous enzymes, where at least one enzyme is an endogenous enzyme (claims 1, 27 and 28). Preferred reporter enzymes are disclosed as luciferase,  $\beta$ -galactosidase ( $\beta$ -gal), glucuronidase, alkaline phosphatase, carboxyl esterase, acid phosphatase and glucosidase (column 6, line 65-column 7, line 1).

The Examples in Bronstein et al. describe the detection of alkaline phosphatase and luciferase with a reagent having a 1,2-dioxetane substrate for alkaline phosphatase and luciferase detection reagents in a sequential assay;  $\beta$ -gal and alkaline phosphatase with a dioxetane containing  $\beta$ -gal substrate and a dioxetane containing alkaline phosphatase substrate in a sequential assay;  $\beta$ -gal, luciferase and alkaline phosphatase with a dioxetane containing  $\beta$ -gal

substrate, luciferase detection reagents and a dioxetane containing alkaline phosphatase substrate in a sequential assay;  $\beta$ -glucosidase and luciferase with a dioxetane containing  $\beta$ -glucosidase substrate and luciferin in a sequential assay; and PLAP and  $\beta$ -glucosidase with a dioxetane containing PLAP substrate and a dioxetane containing  $\beta$ -glucosidase substrate in a sequential assay. No assays which detect fluorogenic and bioluminogenic products are disclosed in Bronstein et al.

Disparate enzyme kinetics, assay chemistries and incubation requirements of various reporter enzymes can complicate combining two reporter enzymes into an integrated, single tube or dual reporter assay format. Notably, neither Grant et al. nor Bronstein et al. disclose or suggest multiplex bioluminogenic and fluorogenic assays for enzyme-mediated reactions. It is only Applicant's specification that provides the reasonable expectation of success for bioluminogenic and fluorogenic multiplex assays.

Accordingly, withdrawal of the § 102(b) and § 103(a) rejections is respectfully requested.

**CONCLUSION**

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney at (612) 373-6959 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

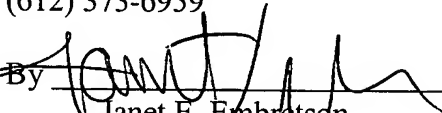
Respectfully submitted,

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Date November 1, 2006

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